

CLAIMS

1) A recombinant~~Recombinant~~ baculovirus constituting comprising an expression vector that can be used for use in the production of immunoglobulins in an insect cell, and characterized in that it comprisessaid expression vector comprising:

—an first expression cassette comprising a first sequence coding for at least one part of an immunoglobulin H chain, which wherein said first sequence is placed under transcriptional control of a first baculovirus promoter,

—an second expression cassette comprising a second sequence coding for at least one part of an immunoglobulin L chain, which wherein said second sequence is placed under transcriptional control of a second baculovirus promoter; wherein the said first baculovirus promoter and the said second baculovirus promoter~~promoters~~ are two different promoters and are located at two different loci.

2) The recombinant~~Recombinant~~ baculovirus in accordance with Claim 1, characterized in thatwherein one of the said first and second baculovirus promoters is located at the site occupied in the wild baculovirus by the polyhedrin promoter and that the other baculovirus promoter is located at the site occupied in the wild baculovirus by the p10 promoter.

3) The recombinant~~Recombinant~~ baculovirus in accordance with Claim 1 or 2, characterized in that the two~~said~~ first and second baculovirus promoters are strong promoters, wherein said strong promoters are at least as strong as a polyhedrin promoter or a p10 promoter.

4) The recombinant~~Recombinant~~ baculovirus in accordance with Claim 3, characterized in thatwherein at least one of the first and second baculovirus promoters is selected from the group constituted by~~consisting~~ of:

- the a p10 promoter;

- the a polyhedrin promoter; and

- a synthetic promoter, referred to as Syn promoter and constituted bycomprising a double-strand stranded DNA fragment the sequence of which, shown in the attached sequence listing as SEQ ID NO.: 1 and SEQ ID NO.: 2, is the following having the following sequences:

5-
ATCAAATAAATAAGTATTTAAAGAATTCTGTACGTATTTGTATATTAATTAAAATCTACTGTAAATAGATCG
TAGTTTATTATTCTAATAAATTTCTAACATGCATAAAACATATAATTAATTATGATATGACATTCTAGCCTAG
3-
-3 (SEQ ID NO:1)
-5 (SEQ ID NO:2)

5) The recombinantRecombinant baculovirus in accordance with one of ClaimsClaim 1 to 4, characterized in thatwherein each of said first and second expression cassette cassettes comprises: (i) a strong baculovirus promoter at least as strong as a polyhedrin or p10 promoter and, under the control of the said promoter: (ii) a sequence coding for a signal peptide; (iii) a sequence coding for a variable immunoglobulin domain; and (iv) a sequence coding for a constant domain of an immunoglobulin H or L chain.

6) The recombinantRecombinant baculovirus in accordance with Claim 5, characterized in that the wherein said sequence coding for a signal peptide placed under the control of the first promoter of said first expression cassette is different from the said sequence coding for a signal peptide placed under the control of the second promoter of said second expression cassette.

7) The recombinantRecombinant baculovirus in accordance with Claim 5 or 6, characterized in that, wherein at least one of the sequences coding for a signal peptide codes for a peptide that has an His-Val-Ser signal immediately upstream of the cleavage site used by the signal peptidase.

8) The recombinantRecombinant baculovirus in accordance with one of ClaimsClaim 5 to 7, characterized in that the sequencewherein at least one of said coding for the a constant immunoglobulin domain is a sequence of human origin.

9) An insect~~Insect~~ cell infected by a recombinant baculovirus in accordance with one of Claims~~Claim 1 to 8~~.

10) A method for preparing an immunoglobulin comprising the steps of: culturing~~Procedure~~ for the preparation of an immunoglobulin, characterized in that insect cells in accordance with Claim 9 are cultured and that the~~extracting~~ said immunoglobulin is extracted from the culture medium.

11) An immunoglobulin~~Immunoglobulin~~, characterized in that it can be obtained by the procedure in accordance with~~method~~ of Claim 10.

12) A process for preparing~~Procedure~~ for the preparation of a recombinant baculovirus in accordance with one of Claims~~Claim 1 to 8~~, which procedure is characterized in that~~comprising the steps of:~~

- one prepares~~preparing~~ a first transfer plasmid comprising a sequence coding for at least one part of an immunoglobulin H chain, under transcriptional control of a first strong baculovirus promoter; ~~at least as strong as a polyhedrin promoter or p10 promoter~~

- one prepares~~preparing~~ a second transfer plasmid comprising ~~the-a~~ sequence coding for at least one part of an immunoglobulin L chain, under transcriptional control of a second strong ~~baculovirus~~ ~~at least as strong as a polyhedrin promoter or p10 promoter of the said baculovirus;~~

- ~~with the~~wherein said first and second promoters being~~are~~ two different promoters;

- one carries out~~the~~ performing homologous recombination of the two plasmids with baculovirus DNA;

- allowing replication of viral DNA in transfected cells;

- after replication of the viral DNA in transfected cells, one proceeds to the selection of~~the~~ selecting recombinant baculoviruses that have integrated~~the~~

sequence coding for at least one part of the immunoglobulin H chain and the sequence coding for at least one part of the immunoglobulin L chain.

13) ~~Procedure in accordance with~~ the process according to Claim 12, characterized in that ~~wherein~~ each of said first and second transfer plasmid ~~used~~plasmids carries an insert comprising:

- an expression cassette such as defined in Claim 5 and, on both sides of this cassette,comprising a strong baculovirus promoter at least as strong as a polyhedrin promoter and, under the control of said promoter, a sequene coding for a signal peptide, a sequence coding for a variable immunoglobulin domain, and a sequence coding for a constant domain of an immunogloulin H or L chain, said expression cassette flanked on each side by baculovirus sequences homologous with those of the regions flanking the portion of the viral genome ~~which it is the intention to replace by insertion of the said cassette being replaced by said expression cassette.~~

14) ~~The process according to~~ procedure in accordance with Claim 13, characterized in that ~~the~~wherein said baculovirus sequences are homologous with ~~these~~sequences of the regions flanking the p10 gene or homologous with those of the regions flanking the polyhedrin gene.

15) ~~The process according to~~ procedure in accordance with Claim 14, characterized in that ~~the~~wherein said baculovirus DNA with which is effected the homologous recombination of the transfer plasmids is constituted bycomprises DNA from a baculovirus that has previously been modified by insertion of ~~two~~having a Bsu36I sit on ~~both~~each side of the sequence coding for the p10 protein (~~these, wherein said two~~ Bsu36I sites ~~being~~are the only Bsu36I sites for the enzyme under consideration in the genome of the said modified baculovirus) DNA and wherein said baculovirus DNA is digested by the enzyme Bsu36I.